

Supplementary Discussion for “Strains, functions, and dynamics in the expanded Human Microbiome Project”

Updated associations between phenotype and microbiome composition

With a ~2.5x increase in the number of different subjects with WMS samples at each targeted body site, we tested for significant correlations between species abundances, pathways, and covariates that the initial HMP dataset was not powered to detect¹ (**Extended Data Fig. 8**; see Methods for included metadata and confounders). Overall, 151 significant associations were found with species abundances (**Extended Data Fig. 8a, Table S11**), and 469 were found with pathways (**Extended Data Fig. 8b, Table S11**). Previously-significant associations persist in the new analysis (**Extended Data Fig. 9d-f**).

A new noteworthy association includes a negative relationship between the abundance of Firmicutes and whether the subject had been breastfed as an infant (**Extended Data Fig. 9a**), which has not been seen in previous adult cohorts (e.g. ref. ²). Interestingly, this is in the opposite direction to recent surveys of the developing infant gut microbiome³. Having been breastfed was also linked to the oral clades *Neisseria* (**Extended Data Fig. 9b**), *Rothia* and *Veillonella*, previously identified to be differentially abundant in breastfed infants versus formula-fed infants⁴; these clades overlapped with oral microbes that also differed with age independently of breastfeeding status (e.g. **Extended Data Fig. 9c**).

References

- 1 The Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. *Nature* 486, 207-214, doi:10.1038/nature11234 (2012).
- 2 Falony, G. et al. Population-level analysis of gut microbiome variation. *Science* 352, 560-564, doi:10.1126/science.aad3503 (2016).
- 3 Chu, D. M. et al. Maturation of the infant microbiome community structure and function across multiple body sites and in relation to mode of delivery. *Nat Med* 23, 314-326, doi:10.1038/nm.4272 (2017).
- 4 Holgerson, P. L. et al. Oral microbial profile discriminates breast-fed from formula-fed infants. *J Pediatr Gastroenterol Nutr* 56, 127-136, doi:10.1097/MPG.0b013e31826f2bc6 (2013).